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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/828,531 | 04/14/2004 | M. Zouhair Atassi | MSC-21947-1-CU | 4293 |

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| EXAMINER | |
|---|---|
| SAUNDERS, DAVID A | |
| ART UNIT | PAPER NUMBER |
| 1644 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 02/14/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/828,531 | ATASSI ET AL. | |
| | Examiner | Art Unit | |
| | David A. Saunders, PhD | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *22-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**AMENDMENT ENTRY**

Amendment of 11-27-06 has been entered. Claims 1-26 are pending. Claims 1-26 are under examination. The amendment has entered no new matter.

**RESPONSE TO ELECTION/RESTRICTION**

Applicant's election without traverse of Group I (claims 1-21) in the reply filed on 11/27/06 is acknowledged.

**OBJECTION(S) TO DISCLOSURE**

Figure 1 should be designated by a legend such as --Prior Art-- because only that which is old is illustrated. See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Figure 1 is considered to show only that which is old because it appears to present merely the same plot as that shown at page 3 of APPENDIX #1, "Analysis of uPA in Supernatants..." (cited on Form 1449). The data was plotted in Dec. 1989 and is thus old.

**OBJECTION(S) TO CLAIMS**

Claim 14 is objected to under 37 CFR 1.75(i), as being of improper form for failing to indent each recited element of the kit. In the "said immunological compositions" paragraph, recitations pertaining to the "first" through "third" peptides require further indentation.

Claim 20 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The immunological composition set forth in claim 20 does not further limit that set forth in claim 14.

**REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH**

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims 1, 11-14 and 21 all recitations of a "peptide corresponding to a sequence" are indefinite because the phrase "corresponding sequences" is not art recognized. One has know idea whether "corresponding" would mean an art accepted, narrow term, such as "identical"; or whether "corresponding" would mean an art accepted, broader term, such as "homologous". Thus the meets and bounds of the claim are unclear.

Claims 1, 11-14 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: Claim 1 is incomplete because it concludes with the step of "determining the quantity of each of said immunological compositions..." and then does not relate how each of the determinations is used to for "determining total urokinase concentration" as stated in the preamble. Like consideration applies to the conclusion of claim 14. In a similar manner, there is no conclusion to the three "determining" steps of claims 11-13 and the "determine" step of claim 21 that relates how each of the determinations is used for "determining total urokinase concentration".

Claims 6-7 and 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See

MPEP § 2172.01. The omitted structural cooperative relationships are: Claim 6 fails to state how "the additional peptide" is actually used. The claim suggests that it is "used to derive said immunological composition" in the singular; however one does not know which of the three immunological compositions of base claim 1 it is that claim 6 may be referring to, or whether there is some fourth immunological composition that claim 6 may be referring to. If the latter case is intended, then one does not know how the fourth immunological composition would be used. Like considerations apply to claim 18 in relation to base claim 14.

In clams 6, 11-13 and 21 reference to "urokinase zymogen" is unclear because one does not know how this relates to the "active and inactive forms of urokinase" recited in the preamble.

In claims 6-7 and 14 "used to derive" is unclear because base claims 1 and 14 have recited "obtaining" not "deriving" immunological compositions.

In claims 11-13 and 21, recitations of "determining the amount" in the last three para. are not consistent with the recitation in the preceding para., of a "quantity" rather than an "amount".

In claims 11 and 12, numerous recitations of "which binds to" are not consistent with the concluding para. base claim 1 which recites "which is bound to" rather than "which binds to".

In claims 13 and 21, recitations of "which binds to" in the last three para. are not consistent with the preceding para., which recites "which is bound to" rather than "which binds to".

In claim 14, in the "said immunological compositions" paragraph, recitation of "a peptide directed against each of a set of peptides" is unclear.

In claim 18 reference to "Seq. ID No. 15 which includes amino acid residues 135 and 136" is unclear because "Seq. ID No. 15" has only 10 amino acid residues.

**REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH**

Claims 9 and 13-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the case wherein the immunological

composition is an antiserum, an antibody, or a supernatant of a hybridoma, obtained via injection into a mammal of said peptide, does not reasonably provide enablement for the case wherein the immunological composition is a hybridoma. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. It is art known that hybridoma cells secrete monoclonal antibodies (e.g. into a supernatant) which are "directed against" an antigen, such as a peptide. It is not, however, art known how to use the hybridoma cells per se as an immunological composition which would be "directed against" any antigen. Therefore the embodiment of instant claims 9, 13, 14 and 20, wherein the immunological composition is a hybridoma, is not enabled.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not adequately described the genus of "immunological compositions".

Applicant has given no definition of the genus, except for the functional definition of being "directed against" one of the peptides. One of skill would interpret the phrase "directed against" to refer to "binding" of an immunological nature (e.g. immunospecific binding). The only members of the genus which applicant has specified are "an antiserum, an antibody, a hybridoma, or a supernatant of a hybridoma, obtained via injection into a mammal of said peptide." However, as noted supra under enablement, it is art known that hybridoma cells per se would not be "directed against" any antigen. That is, hybridoma cells would not fall within the scope of reagents that are capable of immunological binding (let alone immunospecific binding. Since applicant has listed a member that is an improper member of the genus, one cannot picture what else the genus includes, besides an antiserum, an antibody, or a supernatant of a hybridoma, obtained via injection into a mammal of said peptide.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant was not in possession of any "peptide corresponding to" any of the sequences recited in each of claims 1, 11-14 and 21. If a "peptide corresponding to" would encompass more than the recited sequence per se (e.g. if it would encompass homologous sequences), then applicant has not described the full genus of peptides encompassed. Except for the very narrow considerations of what substitutions would be entered in the peptides, as set forth in para. [0020] applicant has not described the structural features of the members of the broader genus. Applicant was not in possession of the full genus of amino acid sequences which would be "homologous" (an art accepted term) or "chiefly derived" (not an art accepted term, which is recited by applicant in para. [0020]) to each of the recited segments of SEQ ID NO:16 and SEQ ID NOS:1-14 which are sub-segments thereof. Since the substitution of a single amino acid within any given parent polypeptide sequence can abolish the binding of an antibody thereto (Lederman et al, Molec. Immunol. 28, 1171-1181, 1991), the use of an antibody directed to a variant sequence that is non-identical to that of any of the disclosed SEQ ID NOS could result in the use of an antibody which lacks any binding specificity for urokinase. Not only could such an antibody lack binding specificity for urokinase, such an antibody could also show a cross reactivity for serine protease proteins which are homologous to urokinase; the assay for total urokinase would thereby give false-positive results.

Applicant has not disclosed what substitutions within any one of the disclosed SEQ ID NOS constitute those which characterize urokinase, as opposed to homologous proteins; and applicant has not given any direction as to which substitutions can be placed within any SEQ ID NO such that an antibody reactive therewith can retain specificity for urokinase. The particularly disclosed sequences of SEQ ID NOS: 1-14 and 16 are thus not representative of the genus of peptides which can induce the

production of antibodies with specificity for ("directed against") urokinase. The only members of the genus which have been described are the particularly recited SEQ ID NOS. See Univ. of Calif. V. Eli Lilly 43 USPQ2d 1398.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of antibodies specific for the particularly recited SEQ ID NOS, does not reasonably provide enablement for the use of antibodies specific for the full genus of peptides which be those "corresponding to" the recited SEQ ID NOS. (assuming that "corresponding to "would be encompass terms such as "homologous" (an art accepted term) or "chiefly derived" (not an art accepted term)). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. As noted supra under description, the members of the genus of peptides which can be those "corresponding to" the recited SEQ ID NOS is large, and the state of the art is such that there has been no identification of the structural features of the peptides which, upon immunization, will generate antibodies specific for urokinase. Therefore the experimentation required to produce the antibodies which would be operative in detecting urokinase would be undue. This fact situation does not parallel that of In re Wands 8USPQ2d 1400. Instantly, one would need to immunize a different host animal with each of the peptides encompassed by the genus and then characterize the antibodies produced by each animal. On the other hand, in Wands one animal had already been immunized, and the experimentation merely required the identification of particular hybridoma cell cultures derived from B-cells of the immunized animal. Given the large number of permutations that could be obtained by substituting an unspecified number of amino acid residues, within each of the recited SEQ ID NOS., it would not be practical for one to immunize all of the animals that would need to be immunized, let alone to conduct the experimental work necessary to characterize the antiserum produced by each of the animals.

**ART OF INTEREST**

The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Morrison (5,869,238) is of interest with respect to known antibodies against urokinase (uPA). See col. 5,lines 6+.

Mazar et al (2005/0232924) is of interest for showing monoclonal antibodies directed against the amino terminal fragment of urokinase (residues 1-143). See para. [0169]-[0171].

**CONTACTS**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 2/5/07 DAS

David A Saunders

DAVID A. SAUNDERS
PRIMARY EXAMINER